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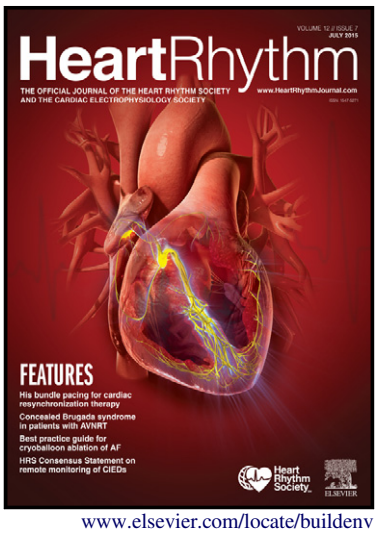

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Larissa Fabritz FESC

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Author: Larissa Fabritz, FESC,

Institute of Cardiovascular Sciences,

College of Medical and Dental Sciences,

University of Birmingham, UK

Edgbaston Birmingham B15 2TT

+44 121 41 48259/46938/47042

L.Fabritz@bham.ac.uk

With increasing life expectancy, the Beatles song "When I'm Sixty-Four" could be changed to "When I'm Ninety-Four" soon. Dementia and stroke, some of the most feared conditions in old age, are often caused by silent atrial fibrillation[1, 2] and may be heralded by changes in the P wave as suggested in the study by Martínez-Sellés et al. (2015)[3] in this volume. The authors focus on P waves in centenarians, over a century after the first description of the P wave. The authors report observations on interatrial block in centenarians with implications well beyond this population.

Interatrial block grade one and two is clearly illustrated in the manuscript and the syndrome and its history described[3]. In short, interatrial block is characterized by a prolonged P wave. P waves with plus/minus biphasic morphology in leads II, III, and aVF reflect that the atrial stimulus is blocked in the upper part of the atrial septum and that activation is caudo-cranial. Bayés de Luna[4] classified these types of atrial block as either a partial block (indicated by a P wave ≥120 ms) or an advanced block (indicated by a P wave ≥120 ms *and* a biphasic pattern in leads II, III, and aVF, Figure 1).

The group collected surface ECG recordings and echocardiography data from 80 Spanish individuals over the age of 100 and performed a follow-up by telephone. P waves were analyzed in each recording and findings compared to controls in their 70s. The study describes the prevalence of interatrial block in centenarians as well as morbidity and mortality during follow up. The authors

concluded that in the centenarians, there was a higher incidence of interatrial block and atrial fibrillation as compared to the septuagenarians. Interestingly, normal atrial activity in the ECG was an exception with the centenarians studied, rather than the norm. Centenarians with interatrial block and atrial fibrillation had mitral insufficiency more often and had previously suffered from stroke more often than other centenarians.

The authors postulate that interatrial block could be a possible marker for stroke risk and a precursor for the development of atrial fibrillation. Morbidity and mortality was highest in patients with atrial fibrillation and intermediate in patients with interatrial block, in comparison to those with normal sinus rhythm and normal P wave duration. This small study therefore has a potentially big impact on prevention and early therapy of atrial fibrillation and stroke.

It is known that as people age, an atrial substrate develops, increasing their susceptibility to arrhythmias. Thus, it is not surprising that centenarians have a higher incidence of interatrial block and atrial fibrillation. However, the fact that only a third of centenarians in this study had a normal P wave is an urgent call for us to start looking out for abnormal P waves and atrial fibrillation in the elderly on a more regular basis. Atrial fibrillation begets atrial fibrillation[5]; the longer it is present, the more difficult it is to treat. Silent atrial fibrillation can damage the myocardium and lead to stroke as a first symptom. In this respect, clinical parameters identifying an individual at high risk of atrial fibrillation are highly wanted[2]. Therefore, the association of interatrial block with atrial fibrillation and stroke described in this study invites us to follow up with immediate action.

A better characterization of the different types of atrial fibrillation can help target therapies more effectively[2]. More mechanistic insights on interatrial block and its relevance for atrial fibrillation and stroke are needed. This observational study is just a beginning. It fosters research opportunities into the mechanisms of ECG changes in the elderly and their association with or even causality of disease and needs confirmation. The observations in this study raise questions to the cardiovascular community as well as to geriatricians, stroke-teams, and scientists in health population sciences: Should ECG screening for P wave length, interatrial block and atrial fibrillation be mandatory for

certain age groups in addition to just taking a patient's pulse? Should screening be intensified and therapeutic measures taken earlier than currently if "pre-atrial fibrillation" alterations in the ECG such as interatrial block with atrial extrasystolies are documented in order to slow cognitive decline and prevent embolisms?

The study has limitations which are discussed by the authors. Although the study is large as compared to previous studies on interatrial block in centenarians, confirmation by both larger and more informed studies is needed. Information on factors known to influence the P wave such as anti-arrhythmic medications, previous ablation, and genetic factors, was not collected in this study. Data on anticoagulation and follow up details were unavailable and potential bias may have arisen from the selection of the centenarians, since some were included on the day of a hospital discharge.

The findings also present questions to basic science researchers: Would an experimental setting with induced interatrial block increase the probability of inducing atrial fibrillation? Would any conduction slowing result in interatrial block and increased inducibility of atrial fibrillation? Apart from age, we know that genetic factors can influence the length of the P wave and the PR interval from large studies[6], with of the many genetic factors, Scn5a and Tbx5 dominating regulation. An association of P wave length and PR interval with atrial fibrillation has been described in populations and GWAS studies[1] as well as in genetic models prone to atrial arrhythmia[7].

There are technical challenges in defining P wave characteristics. Use of digital ECGs with multiple electrode sites needs to be encouraged as they can provide high resolution recordings reflecting processes in the left atrium better. The end of the P wave may not only be hard to define, but reflect the unexpected. For example, the terminal component of the P wave not only represents conduction, but can reflect the beginning of repolarization of the atria. P wave assessment including P terminal force, P1 duration x P amplitude in the Atrial Fibrillation Genetics Consortium consisting of studies in over 20 studies in the US and Europe will hopefully account for interatrial block. Like QRS duration, P wave duration correlates with mortality[3]. We conclude that the ECG still remains as one of our best biomarkers yet.

If the careful observation of the group of Bayes de Luna can be confirmed in large population-based studies, a small wave in the ECG could make a big impact on clinical decision making.

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Figure 1: The Great Wave revisited. "In the well of a wave off Kanagawa", print by Katsushika Hokusai, adapted to depict the prolonged and biphasic P wave in interatrial block.

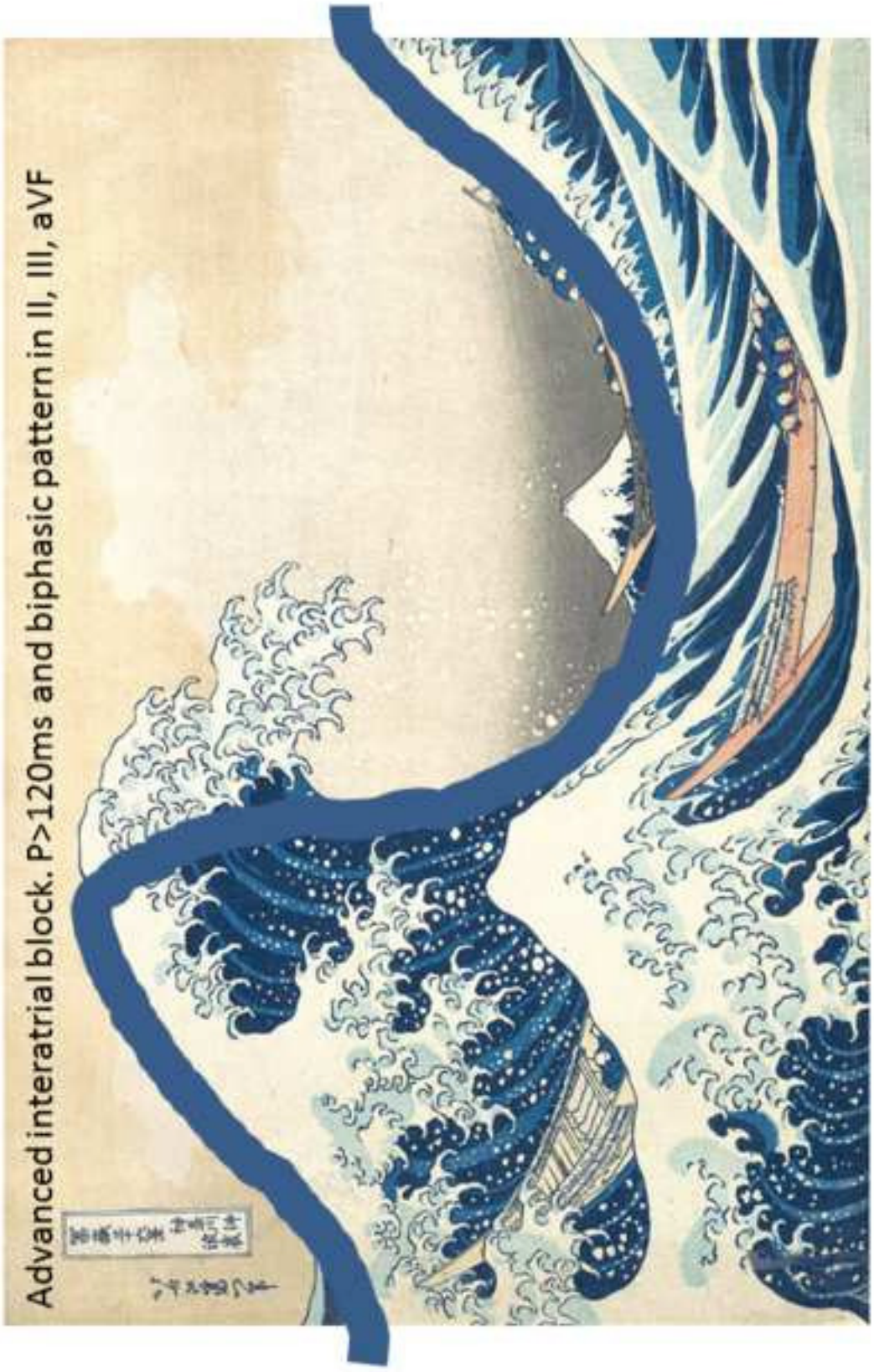

Figure 1